

## **ABSTRACT**

Pharmaceutical compositions and methods of use in regulation of mammalian bone forming activities of sFRPs (secreted frizzled-related proteins) are disclosed. sFRPs are secreted receptors for Wnts, which are important polypeptide growth factors that are known to regulate fundamental biological processes like tissue polarity, embryonic development, and tumorigenesis. A sFRP was isolated from human osteoblast cells and identified as sFRP-1 (also known as SARP-2) and shown to be regulated by osteogenic agents in hOB cells in a differentiation selective manner, modulating the life of osteoblasts/preosteocytes. An sFRP-1 knock-out mouse was generated and deletion of sFRP-1 was found to not affect nonskeletal tissues, skeletal morphology or cortical bone development, while resulting in increased trabecular bone formation, decreased osteoblast and osteocyte apoptosis and increased osteoprogenitor differentiation.